UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/583,642	06/20/2006	Timothy John Norman	07-1007-WO-US	3724

20306 7590 06/10/2009

MCDONNELL BOEHNEN HULBERT & BERGHOFF LLP
300 S. WACKER DRIVE
32ND FLOOR
CHICAGO, IL 60606

EXAMINER	
DICKINSON, PAUL W	

ART UNIT	PAPER NUMBER
1618	

MAIL DATE	DELIVERY MODE
06/10/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/583,642	NORMAN, TIMOTHY JOHN	
	Examiner	Art Unit	
	PAUL DICKINSON	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 March 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4 and 6-10* is/are pending in the application.

4a) Of the above claim(s) *3,4,6 and 9* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,7 and 10* is/are rejected.

7)☒ Claim(s) *8* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3/18/2009 has been entered.

No prior art was found against the elected species. The search was therefore expanded to nonelected embodiments, which is set forth in the prior art rejection below. The search was not extended to the entire scope of the claims since prior art was found for the generic claim. Claims 1-2, 7-8 and 10 are currently under consideration. Claims 3-4, 6 and 9 are withdrawn as not reading on Applicant's elected species or that cited below by the Examiner to reject the claims.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objects are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

New Grounds of Rejection

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

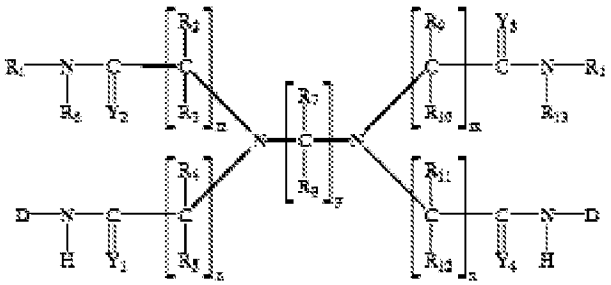
The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-2, 7 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 20020009426 (‘426) in view of WO 2004060965 (WO ‘965). ‘426 discloses

various polyethylene glycol-drug conjugate prodrugs and their pharmaceutical formulations (see abstract; paragraphs 8-46). In one embodiment, the conjugate prodrug has the following structure:



Wherein R_1 may be a polyethylene glycol moiety, R_2, R_3, R_4, R_5, R_6, R_7, R_8, R_9, R_{10}, R_{11}, R_{12} may be hydrogen, Y_1, Y_2, Y_3, Y_4 may be oxygen, D is the residue of a biologically active moiety which may comprise a spacer, m, n and p may be about 1 to about 12 (see page 5, second column, second formula from the top; paragraphs 62-71). The biologically active moiety may be a monoclonal antibody (see paragraph 101). This embodiment of '426 reads on the formula (I) as recited in instant claim 1 as follows:

P^1 and P^2 are a polyethylene glycol moiety;

Z^1 and Z^2 are a polyclonal or monoclonal antibody;

X^1 and X^2 are N;

A^1 and A^2 are NHCO;

B^1 and B^2 are CONH;

V^1 and V^2 are $(CH_2)_v$ wherein, through routine experimentation, one would arrive at the instantly claimed values of v = 1, 2, 3 or 4, see explanation below;

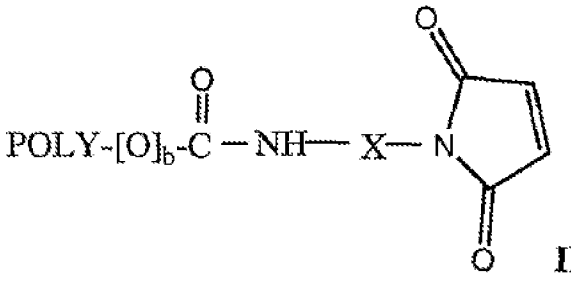
W^1 and W^2 are $(CH_2)_w$ wherein, through routine experimentation, one would arrive at the instantly claimed values of w = 1, 2, 3 or 4, see explanation below;

M^1 is $(CH_2)_m$ wherein, through routine experimentation, one would arrive at the instantly claimed values of m = 1, 2 or 3, see explanation below; and

n = 0.

Regarding instantly recited Y^1 and L^1, although '426 discloses the presence of a spacer between the nitrogen and the biologically active moiety (see paragraphs 54 and 69-71), '426 fails to disclose a spacer of the formula $(CH_2)_y$-maleimide moiety, which would correspond to $Y^1 = (CH_2)_y$ and L^1 = a maleimide moiety as recited in instant claim 1. Similarly, '426 fails to disclose $Y^2 = (CH_2)_y$ and L^2 = a maleimide moiety as recited in instant claim 1. '426 teaches, however, selection of a spacer appropriate to the biologically active moiety used (see paragraphs 69-71). In the case where monoclonal antibodies are used as the biologically active moiety, one of ordinary skill would look in the art for appropriate monoclonal antibody-polymer conjugate spacers.

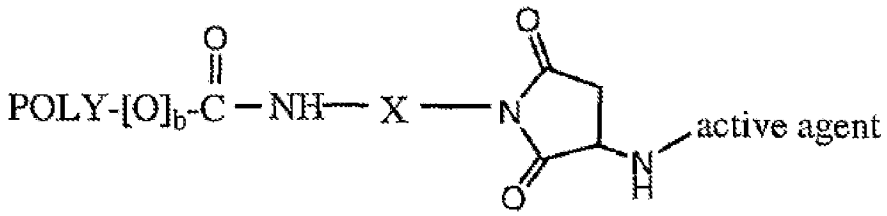
WO '965 discloses maleimide-functionalized polymer precursors and their drug conjugates (see abstract). The maleimide-functionalized polymer precursors generally have the formula:



II.

Where X is a hydrolytically stable linkage such as $(CH_2)_x$ wherein x can be 1, 2, 3, 4, 5 or 6 (see page 4, lines 9-24). Lower case x corresponds to instant y. The

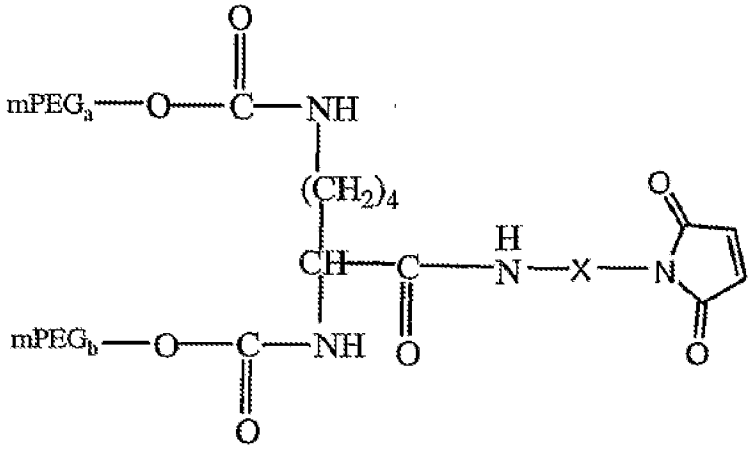
precursor can be bioconjugated with a variety of nitrogen containing protein active agents, including monoclonal antibodies:



XV.

(see page 50, lines 12-19; page 56, lines 29-34)

In some embodiments, the polymer precursor contains multiple polyethylene glycol polymer chains, analogous to the structure disclosed by '426.



XVII

(see page 39, line 20 to page 40, line 16). Thus, $(CH_2)_x$-maleimide moiety serves as a suitable spacer between monoclonal antibodies to polymer precursors, particularly precursors wherein the $(CH_2)_x$-maleimide moiety is bonded to the precursor through -

CONH- (see page 3, lines 4-31). Such prodrugs, relative to their non-pegylated counterparts, possess longer circulatory times in the body due to increased resistance to proteolytic degradation, increased thermostability, and in the case of antibodies particularly, increased bioefficacy (see page 1, line 29 to page 2, line 2).

It would have been obvious to one of ordinary skill in the art at the time the instant invention was made to combine the disclosures of '426 and WO '965 to arrive at the instant invention. Specifically, it would have been obvious to use the $(CH_2)_x$-maleimide spacer of WO '965 as the spacer of '426. The art recognizes this spacer as an appropriate spacer between monoclonal antibodies and polymer precursors, particularly precursors wherein the $(CH_2)_x$-maleimide moiety is bonded through CONH-, as would be the case in the formula of '426 above. Accordingly, the $(CH_2)_x$-maleimide spacer is a suitable spacer for incorporation into the formula of '426 to link the monoclonal antibody to the polymer. The antibody prodrug thus made may possess long circulatory times in the body, high thermostability, and high bioefficacy, all desirable traits for monoclonal antibody drugs. Regarding the parameters m, v and w of the instant claims, it would have been obvious to optimize these parameters, through routine experimentation, to improve the efficacy of the drug. In this way, one would find Applicant's claimed values. The rationale for this is that the range of p of '426 (which corresponds to instant m) of about 1 to about 12 fully encompasses the presently claimed values of m = 1, 2, or 3. Similarly, the range of n of '426 (which corresponds to instant v) of about 1 to about 12 fully encompasses the presently claimed values of v = 1, 2, 3 or 4. The range of m of '426 (which corresponds to instant w) of about 1 to about

12 fully encompasses the presently claimed values of w = 1, 2, 3 or 4. See MPEP § 2144.05, II.

Allowable Subject Matter

Claim 8 is objected to as being dependent upon a rejected base claim, but, to the extent that it reads on the elected species, the claim would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. Claim 8 has been examined only to the extent that it reads on the elected species because prior art was found for the generic claim (see above).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to PAUL DICKINSON whose telephone number is (571)270-3499. The examiner can normally be reached on Mon-Thurs 9:00am-6:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/
Supervisory Patent Examiner, Art Unit 1618

Paul Dickinson
Examiner
AU 1618

June 5, 2009